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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,383	12/22/2000	Peter Van Vlasselaer	03102.0011.NPUS01	9470

27194 7590 12/29/2005

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EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT PAPER NUMBER

1647

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/747,383	<b>Applicant(s)</b> VLASSELAER ET AL.	
	<b>Examiner</b> Jegatheesan Seharaseyon, Ph.D	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 16-23 and 25-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-23 and 25-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/06/2005 has been entered. An action on the RCE follows.
2. Claims 16, 17, 19, 21, 22 and 23 have been amended. Claim 24 has been cancelled. New claims 25-28 have been added. Therefore, Claims are 16-23 and 25-28 are pending and the subject of this action.
3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 103, maintained***

4. The rejection of claims 16-23 and 25-28 (newly added) under 35 USC 103(a) as being unpatentable over Huland et al. in view of both Debs et al. and Ruskewicz et al. further evidenced by Nayar et al or Hora et al. is maintained for reasons stated in the previous Office Action dated 1/13/03, 11/17/03, 10/29/04 and 6/29/05. Applicant arguments have been fully considered but are deemed not to be persuasive. Applicants contend that claim 22 as amended is not taught by the references. Applicants assert that neither Huland nor Debs provides a composition of  $\gamma$ -IFN over the presently claimed defined particle size ranges. It is also asserted that neither Nayar nor Hora describe an aerosol composition over the presently claimed particle size ranges recited in claim 22. In addition, Applicants contend that Ruskewicz reference does not teach or suggest the

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claimed particle size range of: (i) less than 1 micron, (ii) 1-3 microns, (iii) 3-5 microns, (iv) 5-10 microns, or (v) greater than 10 microns. However, Ruskewicz reference as acknowledged by the Applicants in their response dated 10/6/05 page does teach "an aerosol preferably having a particle size in the range of about 1 to 12 microns, more preferably of about 3.0 to 6.0 microns." In addition, Ruskewicz reference also teaches aerosol particles that are in the size range of about 0.5 to 12 microns (column 17, lines 34-36). Therefore, absent evidence to the contrary particle sizes of less than 1 micron, 1-3 microns, 3-5 microns and 5-10 microns are all obvious over the prior art especially in light of the fact that Ruskewicz teach "about." 3-5 microns for example, could be considered "about 3-6 micron". If the term about was taken to mean 10% variation, that would mean a range of 3 to 5.4 micron. This rounded to 2 significant figures as recited in the present invention, that would encompass 3-5 micron. Thus contrary to Applicants assertion references in combination make the instant invention obvious over prior art.

Applicants assertion that the cited references does not teach or suggest claimed retention of substantially the same biological activity, the Office discussed extensively in the Office Action dated 10/29/04 on page 3 that "Debs et al. reference teaches the use of aerosolized IFN-gamma to stimulate alveolar macrophage and blood monocyte function (abstract). It also discusses that IFN-gamma activates macrophages to release IL-1, express class II HLA (Ia) surface Ag, and lyse tumor cells. Therefore, clearly demonstrating that the IFN-gamma biological activity in the aerosol composition is substantially the same as that of the solution. In addition, Debs et al. provide an

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analysis of rHuTNF-  $\alpha$  recovered as a condensate after aerosolization demonstrated that it retained full biological activity, as indicated by migration non-denaturing gels (page 3487, 3<sup>rd</sup> paragraph) and by the ability to growth inhibit tumor cell *in vitro*.

Therefore, absent evidence to the contrary it is assumed that the cytokine activity of the aerosol compositions is substantially the same as that of solution. Further, it should be noted that, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).” Though the Applicants contend that that the Debs reference does not measure the biological activity of  $\gamma$ -IFN, as discussed above it does teach measuring of rHuTNF-  $\alpha$  (also a member of the cytokine family) biological activity to demonstrate that it contains the full biological activity after aerosolization (page 3487, 3<sup>rd</sup> paragraph). Absent evidence to the contrary it would be expected that this biological activity to be substantially same to the aqueous solution.

With reference Applicants assertion that the cited references does not teach or suggest claimed retention of substantially the same molecular size distribution, the Office previously discussed extensively in the Office Action dated 11/17/03 on pages 3-4 the molecular size distribution. Again, Ruskewicz et al. teach that the size of the particles be in the range 0.5 to 12 microns, mean particle size be within a narrow range, so that 80% or more of the particles being delivered to the patient (limitation of new claim 22) have a particle diameter that is within  $\pm 20\%$  of the average particle size, preferably within  $\pm 10\%$ , and more preferably within  $\pm 5\%$  of the average particle size

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(column 17, lines 45-50). **Thus, meeting the limitation of  $\gamma$ -IFN molecular size distribution substantially the same as that aqueous solution.** It is noted that particles within  $\pm 5\%$  of the average is considered within two standard deviations of the mean. This also meets the limitation recited in claim 23, wherein at least 95% of the droplets have a size in the selected size range. Furthermore, Applicant discusses limitations not present in the instant claims with respect to dimerization or aggregation of gamma-interferon and its effect on aerosolization. Therefore, rejection of claims 16-23 and 25-28 (newly added) under 35 U.S.C. 103(a) as being unpatentable over Huland et al. (U. S. Patent No. 5,780,012) in view of both Debs et al. (J.of Imm. Vol. 140: 3482-3488) and Ruskewicz et al. (U. S. Patent No. 5,971,951) is maintained.

5. The rejection of claims 16-23 and 25-28 (newly added) under 35 USC 103(a) as being unpatentable over Huland et al. and Jaffe et al. in view of both Debs et al. and Ruskewicz et al. further evidenced by Nayar et al or Hora et al. is maintained for reasons stated in the previous Office Action dated 10/29/04 and 6/29/05. Applicants' arguments have been fully considered but are deemed not to be persuasive. Applicants' traverse the rejection essentially for the same reasons as stated above in paragraph 4. Thus, the rejection is maintained for reasons stated previously and above in paragraph 4.

***Claim Rejections - 35 USC § 112, first paragraph (New matter) withdrawn.***

6. The rejection of claims 22 under 35 USC 112, first paragraph as failing to comply with written description requirement is withdrawn because Applicants have amended the claims to remove new matter.

***Claim Rejections - 35 USC § 112, second paragraph(new)***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-23 and 25-28 (newly added claims) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claim 22 is rejected as being vague and indefinite in the recitation of the term "selected  $\gamma$ -IFN biological activity". It is unclear how one will select a specific  $\gamma$ -IFN activity such as stimulate CD64. Claims 16-21, 23 and 25-28 are rejected insofar as they depend on rejected claim 22.

7b. Claim 22 is rejected as being vague and indefinite in the recitation of the term "biological activity substantially the same". It is unclear if this means the activity is same or within a range. Claims 16-21, 23 and 25-28 are rejected insofar as they depend on rejected claim 22.

7c. Claim 22 is rejected as being vague and indefinite in the recitation of the term "molecular size distribution substantially the same". It is unclear if this means the size is same or within a limited acceptable range. Claims 16-21, 23 and 25-28 are rejected insofar as they depend on rejected claim 22.

8. No claims are allowable.

***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 12/05

  
**ROBERT S. LANDSMAN, PH.D**  
**PRIMARY EXAMINER**